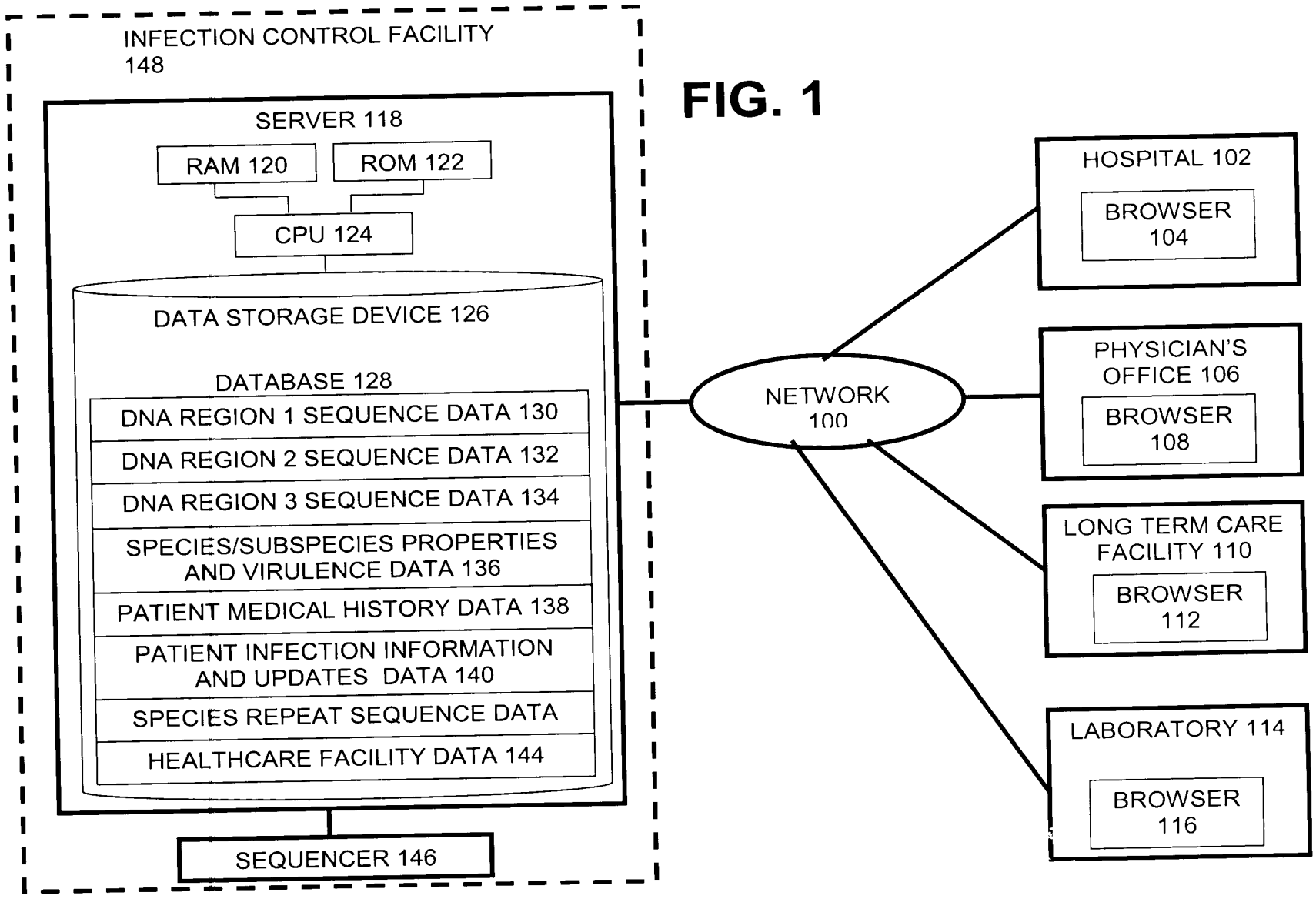
INFECTION CONTROL FACILITY
148
SERVER 118
RAM 120
ROM 122
CPU 124
DATA STORAGE DEVICE 126
DATABASE 128
DNA REGION 1 SEQUENCE DATA 130
DNA REGION 2 SEQUENCE DATA 132
DNA REGION 3 SEQUENCE DATA 134
SPECIES/SUBSPECIES PROPERTIES AND VIRULENCE DATA 136
PATIENT MEDICAL HISTORY DATA 138
PATIENT INFECTION INFORMATION AND UPDATES DATA 140
SPECIES REPEAT SEQUENCE DATA
HEALTHCARE FACILITY DATA 144
SEQUENCER 146
NETWORK 100
HOSPITAL 102
BROWSER 104
PHYSICIAN'S OFFICE 106
BROWSER 108
LONG TERM CARE FACILITY 110
BROWSER 112
LABORATORY 114
BROWSER 116

FIG. 1

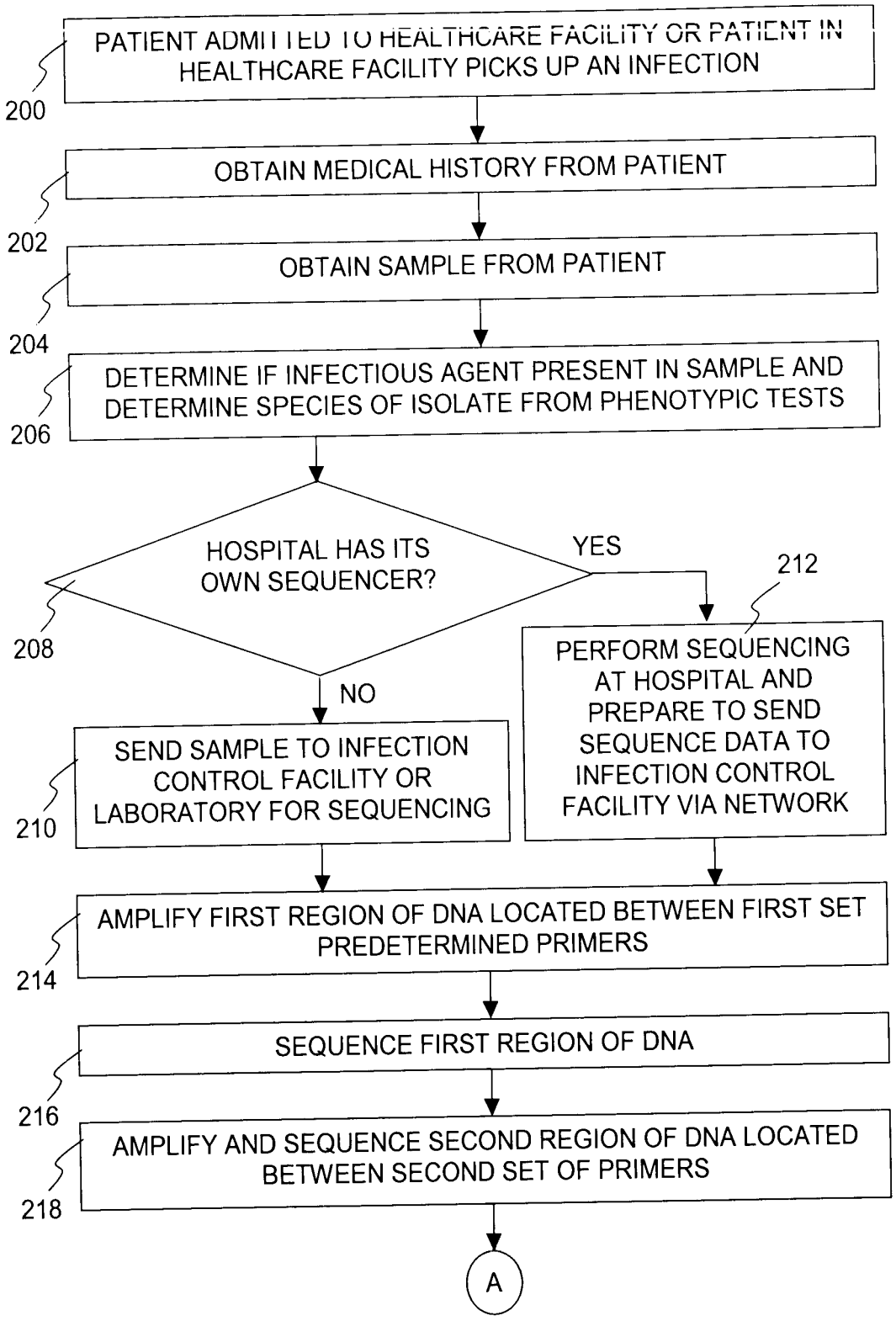
PATIENT ADMITTED TO HEALTHCARE FACILITY OR PATIENT IN HEALTHCARE FACILITY PICKS UP AN INFECTION
200
OBTAIN MEDICAL HISTORY FROM PATIENT
202
OBTAIN SAMPLE FROM PATIENT
204
DETERMINE IF INFECTIOUS AGENT PRESENT IN SAMPLE AND DETERMINE SPECIES OF ISOLATE FROM PHENOTYPIC TESTS
206
HOSPITAL HAS ITS OWN SEQUENCER?
208
YES
212
PERFORM SEQUENCING AT HOSPITAL AND PREPARE TO SEND SEQUENCE DATA TO INFECTION CONTROL FACILITY VIA NETWORK
NO
SEND SAMPLE TO INFECTION CONTROL FACILITY OR LABORATORY FOR SEQUENCING
210
AMPLIFY FIRST REGION OF DNA LOCATED BETWEEN FIRST SET PREDETERMINED PRIMERS
214
SEQUENCE FIRST REGION OF DNA
216
AMPLIFY AND SEQUENCE SECOND REGION OF DNA LOCATED BETWEEN SECOND SET OF PRIMERS
218
A

FIG. 2A

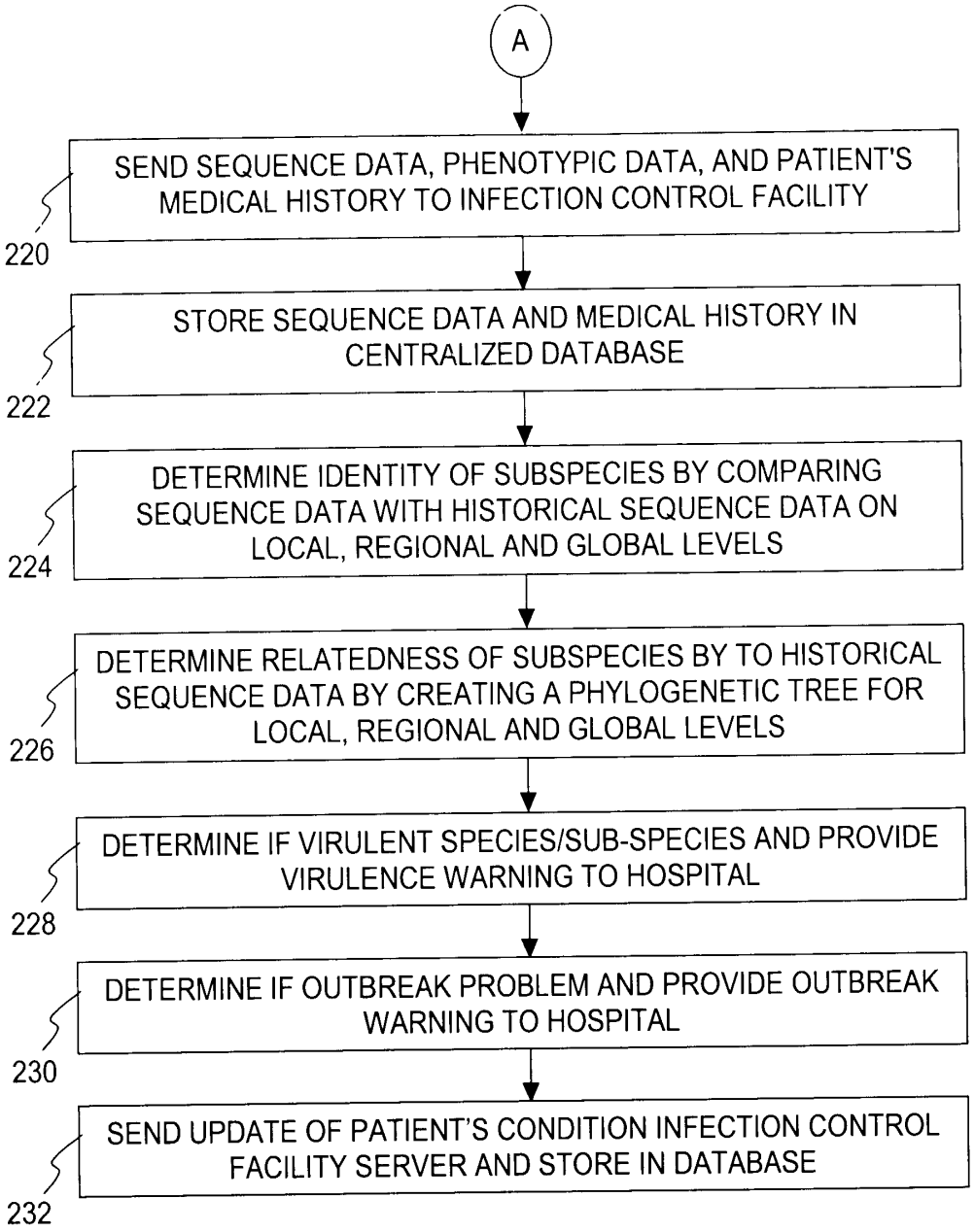
A
SEND SEQUENCE DATA, PHENOTYPIC DATA, AND PATIENT'S MEDICAL HISTORY TO INFECTION CONTROL FACILITY
220
STORE SEQUENCE DATA AND MEDICAL HISTORY IN CENTRALIZED DATABASE
222
DETERMINE IDENTITY OF SUBSPECIES BY COMPARING SEQUENCE DATA WITH HISTORICAL SEQUENCE DATA ON LOCAL, REGIONAL AND GLOBAL LEVELS
224
DETERMINE RELATEDNESS OF SUBSPECIES BY TO HISTORICAL SEQUENCE DATA BY CREATING A PHYLOGENETIC TREE FOR LOCAL, REGIONAL AND GLOBAL LEVELS
226
DETERMINE IF VIRULENT SPECIES/SUB-SPECIES AND PROVIDE VIRULENCE WARNING TO HOSPITAL
228
DETERMINE IF OUTBREAK PROBLEM AND PROVIDE OUTBREAK WARNING TO HOSPITAL
230
SEND UPDATE OF PATIENT'S CONDITION INFECTION CONTROL FACILITY SERVER AND STORE IN DATABASE
232

FIG. 2B

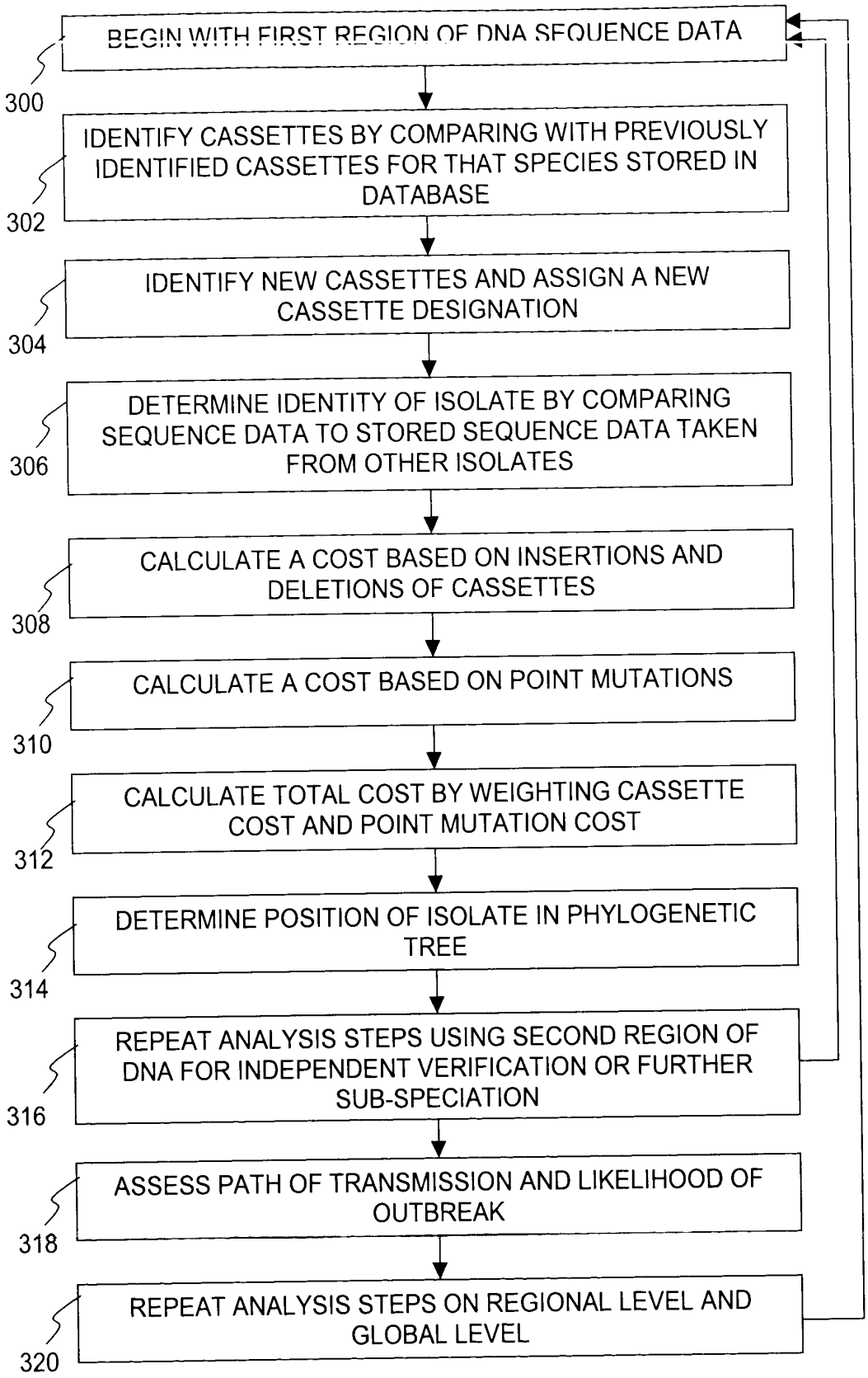
BEGIN WITH FIRST REGION OF DNA SEQUENCE DATA
300
IDENTIFY CASSETTES BY COMPARING WITH PREVIOUSLY IDENTIFIED CASSETTES FOR THAT SPECIES STORED IN DATABASE
302
IDENTIFY NEW CASSETTES AND ASSIGN A NEW CASSETTE DESIGNATION
304
DETERMINE IDENTITY OF ISOLATE BY COMPARING SEQUENCE DATA TO STORED SEQUENCE DATA TAKEN FROM OTHER ISOLATES
306
CALCULATE A COST BASED ON INSERTIONS AND DELETIONS OF CASSETTES
308
CALCULATE A COST BASED ON POINT MUTATIONS
310
CALCULATE TOTAL COST BY WEIGHTING CASSETTE COST AND POINT MUTATION COST
312
DETERMINE POSITION OF ISOLATE IN PHYLOGENETIC TREE
314
REPEAT ANALYSIS STEPS USING SECOND REGION OF DNA FOR INDEPENDENT VERIFICATION OR FURTHER SUB-SPECIATION
316
ASSESS PATH OF TRANSMISSION AND LIKELIHOOD OF OUTBREAK
318
REPEAT ANALYSIS STEPS ON REGIONAL LEVEL AND GLOBAL LEVEL
320

FIG. 3

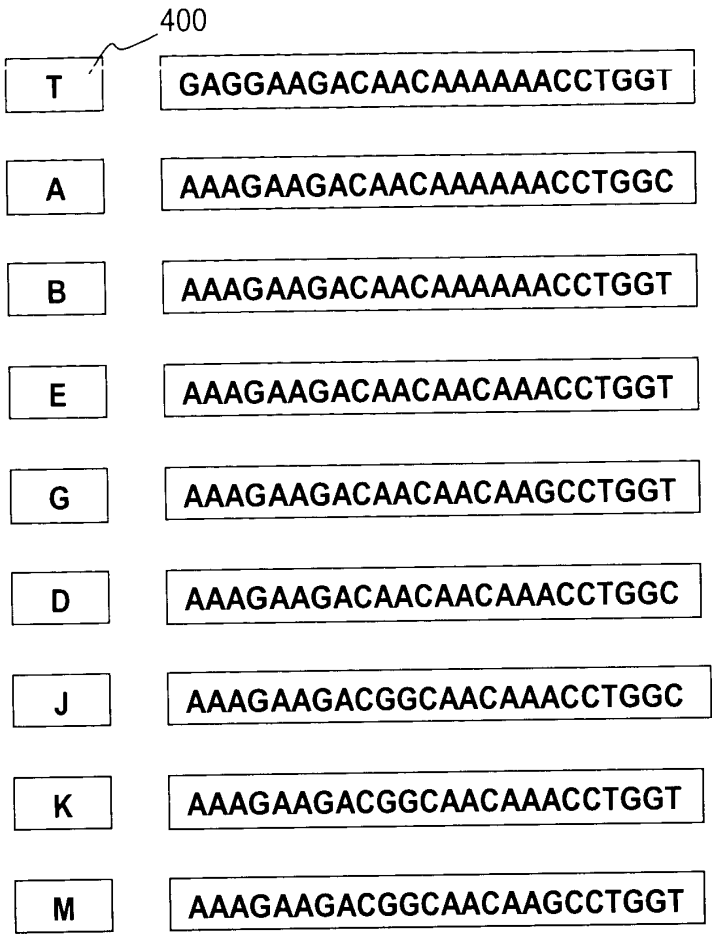
400
T
GAGGAAGACAACAAAAAACCTGGT
A
AAAGAAGACAACAAAAAACCTGGC
B
AAAGAAGACAACAAAAAACCTGGT
E
AAAGAAGACAACAACAAACCTGGT
G
AAAGAAGACAACAACAAGCCTGGT
D
AAAGAAGACAACAACAAACCTGGC
J
AAAGAAGACGGCAACAAACCTGGC
K
AAAGAAGACGGCAACAAACCTGGT
M
AAAGAAGACGGCAACAAGCCTGGT

FIG. 4A

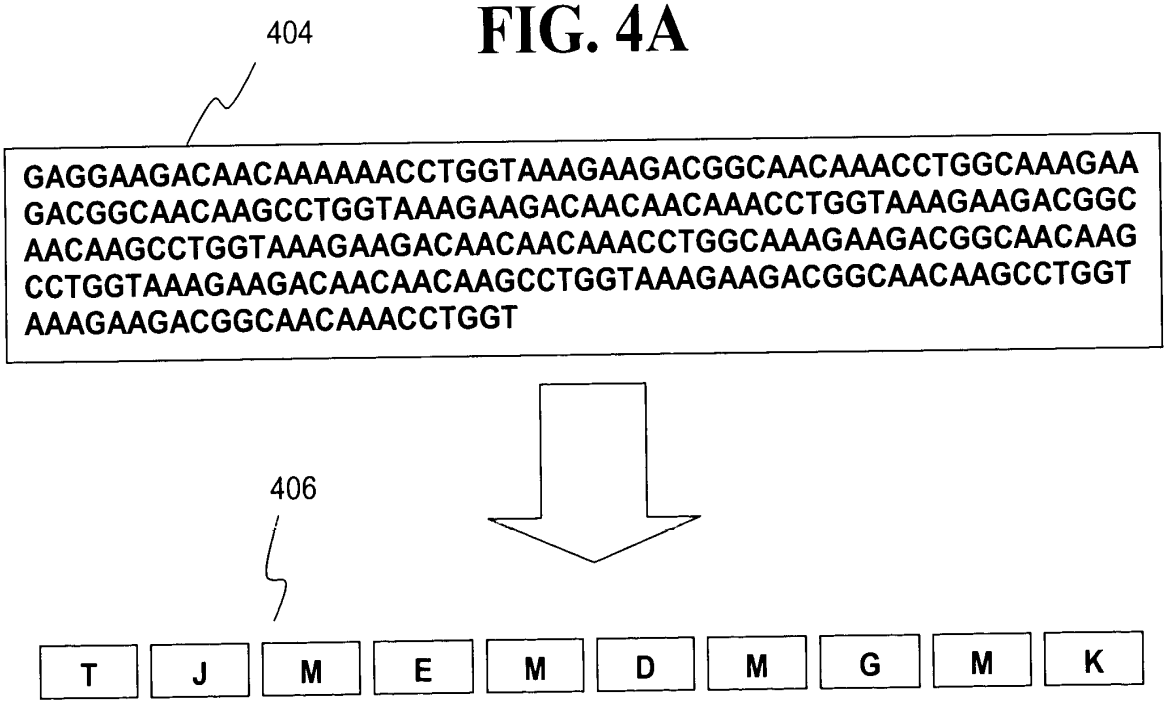
404
GAGGAAGACAACAAAAAACCTGGTAAAGAAGACGGCAACAAACCTGGCAAAGAA
GACGGCAACAAGCCTGGTAAAGAAGACAACAACAAACCTGGTAAAGAAGACGGC
AACAAGCCTGGTAAAGAAGACAACAACAAACCTGGCAAAGAAGACGGCAACAAG
CCTGGTAAAGAAGACAACAACAAGCCTGGTAAAGAAGACGGCAACAAGCCTGGT
AAAGAAGACGGCAACAAACCTGGT
406
T
J
M
E
M
D
M
G
M
K

FIG. 4B

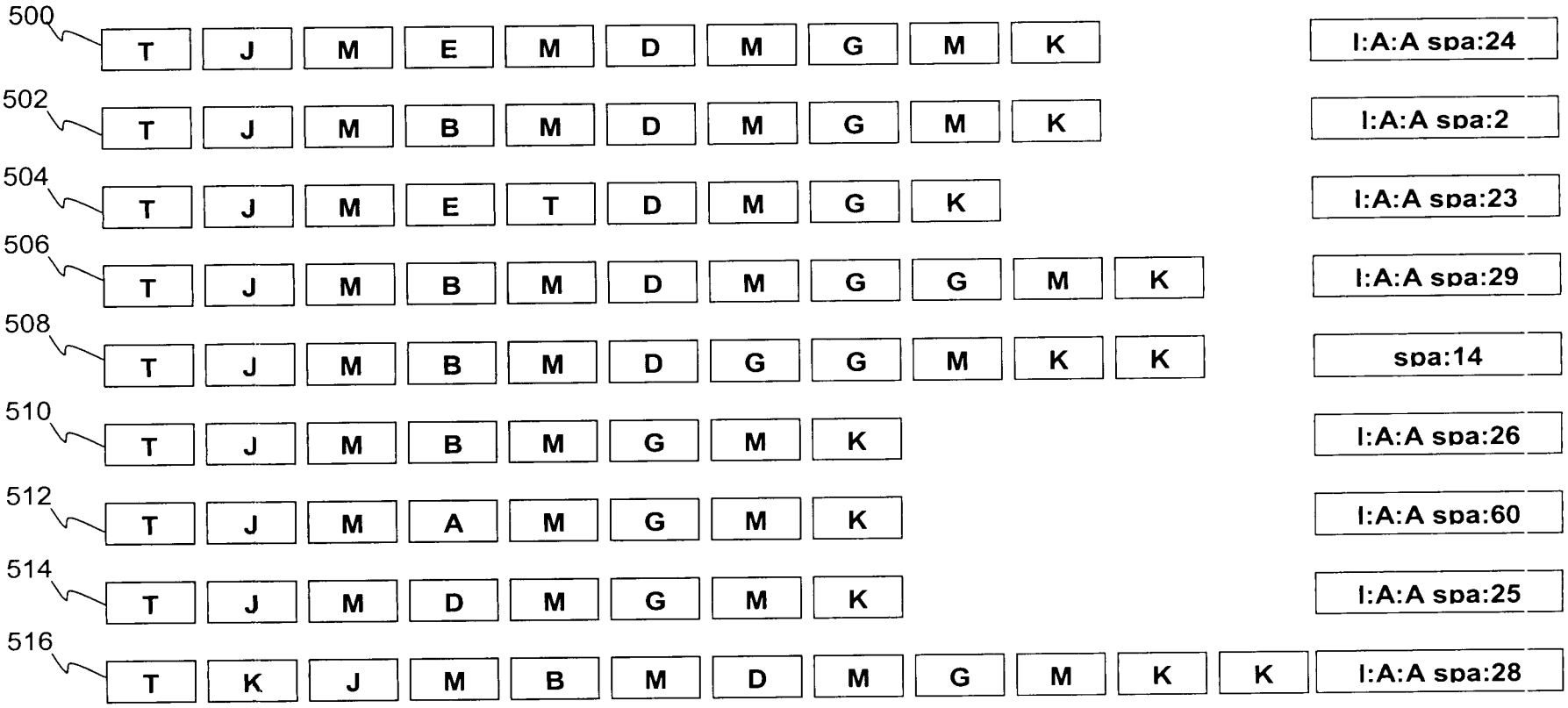
500
T J M E M D M G M K
I:A:A spa:24
502
T J M B M D M G M K
I:A:A spa:2
504
T J M E T D M G K
I:A:A spa:23
506
T J M B M D M G G M K
I:A:A spa:29
508
T J M B M D G G M K K
spa:14
510
T J M B M G M K
I:A:A spa:26
512
T J M A M G M K
I:A:A spa:60
514
T J M D M G M K
I:A:A spa:25
516
T K J M B M D M G M K K
I:A:A spa:28

FIG. 5

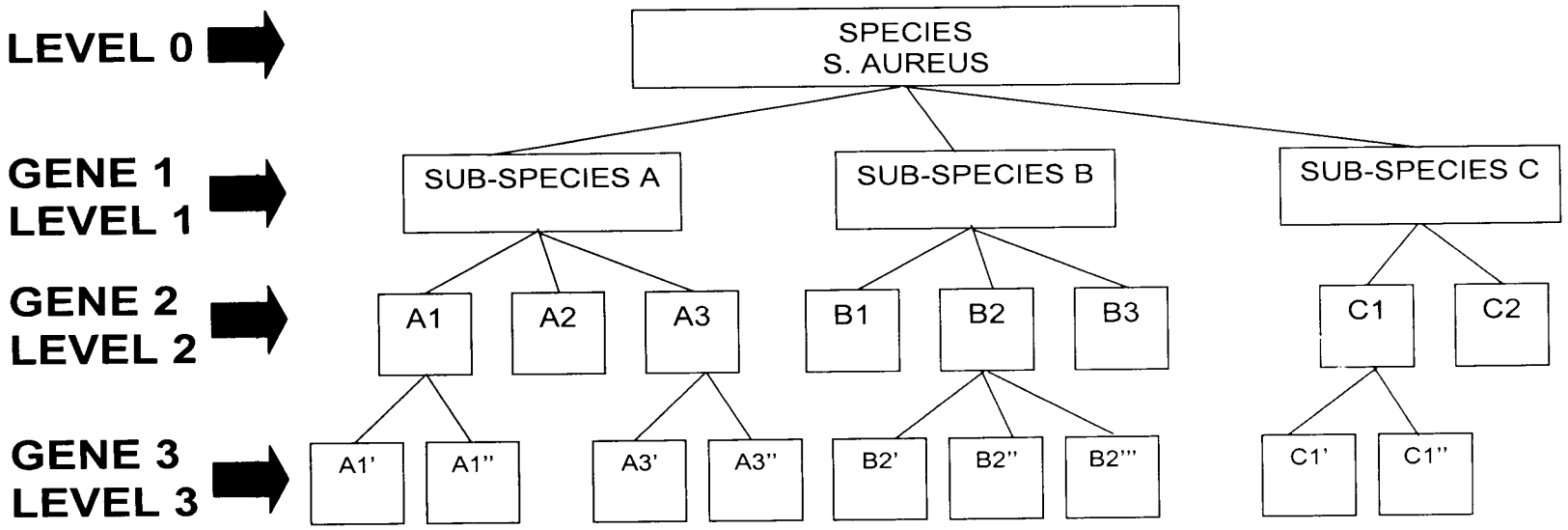
LEVEL 0
GENE 1
LEVEL 1
GENE 2
LEVEL 2
GENE 3
LEVEL 3
SPECIES
S. AUREUS
SUB-SPECIES A
SUB-SPECIES B
SUB-SPECIES C
A1
A2
A3
B1
B2
B3
C1
C2
A1'
A1''
A3'
A3''
B2'
B2''
B2'''
C1'
C1''

FIG. 6

SPECIES	S. aureus	S. aureus	
SUBSPECIES	A1'	B7"	
SEQ REGION 1	ATTCATAGAT...		
SEQ REGION 2	CGTACTATCC...		
SEQ REGION 3	ATTCGTTATA...		
REGION 1 PRIMERS			
REGION 2 PRIMERS			
REGION 3 PRIMERS			
REPEATS REGION 1	TKJMP..		
REPEATS REGION 2	ABABA		
REPEATS REGION 3	TYYT		
DATE	June 5, 2000		
PATIENT MEDICAL HISTORY	Hospitalized in New York Hospital, June 2000 for 3 weeks, heart surgery...		
PATIENT MEDICAL UPDATE INFO	Patient hospitalized 3 weeks for infection and released....	Patient died due to infection after two weeks...	
LOCATION	Mt. Sinai Hospital, Toronto, Burn Ward	New York City Hospital, ICU	
PHAGE TTYPE			

FIG. 7A

S. AUREUS			
SEQ REGION	REPEAT 1	REPEAT 2	REPEAT 3
PROTEIN A X_R	AATTCGCCTAGG.. ..	AATTCCCCTAGG..	TAGGCCGT...
REGION 2	TTAAAGGCCTGA.. .	GGTTCCAATAAT..	GGTTAACC..
REGION 3			

FIG. 7B

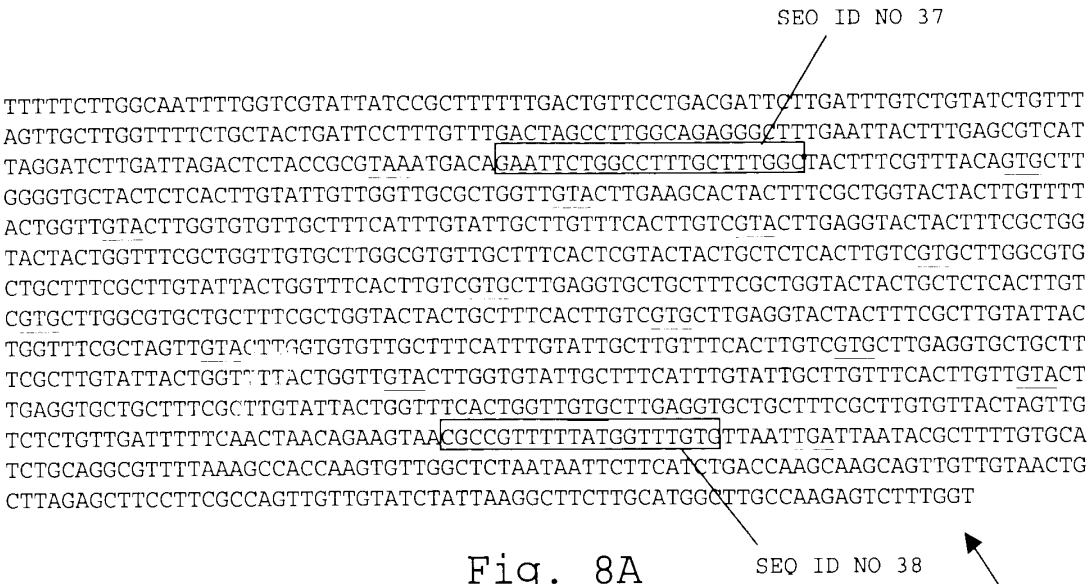

Fig. 8A

GTGCTTGGGGTGCTACTCTCACTTGTATTGTTGGTTGCGCTGGTT SEQ ID NO 24
GTACTTGAAGCACTACTTTCGCTGGTACTACTTGTTTTACTGGTT SEQ ID NO 25
GTACTTGGTGTGTTGCTTTCATTTGTATTGCTTGTTTCACTTGTC SEQ ID NO 26
GTACTTGAGGTACTACTTTCGCTGGTACTACTGGTTTCGCTGGTT SEQ ID NO 27
GTGCTTGGCGTGTTGCTTTCACTCGTACTACTGCTCTCACTTGTC SEQ ID NO 28
GTGCTTGGCGTGCTGCTTTCGCTTGTATTACTGGTTTCACTTGTC SEQ ID NO 29
GTGCTTGAGGTGCTGCTTTCGCTGGTACTACTGCTCTCACTTGTC SEQ ID NO 30
GTGCTTGGCGTGCTGCTTTCGCTGGTACTACTGCTTTCACTTGTC SEQ ID NO 31
GTGCTTGAGGTACTACTTTCGCTTGTATTACTGGTTTCGCTAGTT SEQ ID NO 32
GTACTTGGTGTGTTGCTTTCATTTGTATTGCTTGTTTCACTTGTC
GTGCTTGAGGTGCTGCTTTCGCTTGTATTACTGGTTTTACTGGTT SEQ ID NO 33
GTACTTGGTGTATTGCTTTCATTTGTATTGCTTGTTTCACTTGTT SEQ ID NO 34
GTACTTGAGGTGCTGCTTTCGCTTGTATTACTGGTTTCACTGGTT SEQ ID NO 35
GTGCTTGAGGTGCTGCTTTCGCTTGTGTTACTAGTTGTCTCTGTT SEQ ID NO 36

SEQ ID NO. 23

Fig. 8B

MTEFWPLLWLLSFT
VLGVLLSLVLLVALV SEQ ID NO 39
VLEALLSLVLLVLLV SEQ ID NO 40
VLGVLLSFVLLVSLV SEQ ID NO 41
VLEVLLSLVLLVSLV SEQ ID NO 42
VLGVLLSLVLLVSLV SEQ ID NO 43
VLGVLLSLVLLVSLV
VLEVLLSLVLLLSLV SEQ ID NO 44
VLGVLLSLVLLLSLV SEQ ID NO 45
VLGVLLSLVLLVSLV
VLGVLLSFVLLVSLV
VLEVLLSLVLLVLLV SEQ ID NO 46
VLGVLLSFVLLVSLV SEQ ID NO 47
VLEVLLSLVLLVSLV
VLEVLLSLVLLVVSV SEQ ID NO 48
DFSTNRSNAVFMVCVN

Fig. 8C

SEQ ID NO 51

ATGTTCCAGCCCCTATTAGACGCTTATACAGACAGCACCCGTTTAGATGAAACCGATTATAAGCCCCCATTAAATAT
AGCCCTAGCCAATTGGTGGCCTTTGGATAAAAGAGAAAGCAAAGGGTTTAGGCGTTTTATCTTGTATTTCATCTTAA
GCCAACGCTACACAATCACCCTCCACCAAAACCCTAACGAACCCTCCGATCTTGTCTTTGGCAGTCCTATTGGATCA
GCCAGAAAAATCCTATCCTATCAAAACACTAAAAGGGTGTTTTACACCGGTGAAAATGAAGTCCCTAATTTCAATCT
CTTTGATTACGCCATAGGCTTTGATGAATTGGACTTTAGAGATCGTTATTTGAGAATGCCTTTATATTACGCTAGCT
TGCATTATAAAGCCGAGAGCGTGAATGACACCACCGCGCCCTACAAACTCAAAGACAACAGCCTTTATGCTTTAAAA
AAGCCCTCCCATCATTTTAAAGAAAACCACCCTAATTTATGCGCAGTAGTGAATGATGAGAGCGATCCTTTGAAAAG
AGGGTTTGCGAGCTTTGTCGCGAGCAACCCTAACGCTCCTATAAGGAACGCTTTCTATGACGCTTTAAATTCTATTG
AGCCAGTTACTGGGGGAGGGAGCGTGAAAAACACTTTAGGCTATAACGTCAAAAACAAGAGCGAGTTTTTAAGCCAA
TACAAATTCAATCTGTGTTTTGAAAACACTCAAGGCTATGGCTATGTAACTGAAAAAATCATTGACGCTTATTTCAG
CCACACCATTCCCATTTATTGGGGGAGTCCTAGCGTGGCGAAAGACTTTAACCCTAAGAGTTTTGTGAACGTTTGTG
ATTTTAAAAACTTTGATGAAGCGATTGATTACGTGAGATACTTGCACACGCACCCAAACGCTTATTTAGACATGCTC
TATGAAAACCCTTTAAACACCCTTGATGGGAAAGCTTACTTTTACCAAAATTTGAGTTTTAAAAAAATCCTAGATTT
TTTTAAAACGATTTTAGAAAACGACACGATCTATCACGATAACCCTTTCATTTTCTATCGCGATTTGAATGAGCCTT
TAGTAGCTATTGATGATTTGAGGGTTAATTATGATGATTTGAGGGTTAATTATGATGATTTGAGGGTTAATTATGAT
GATTTGAGGGTTAATTATGATGATTTGAGGGTTAATTATGATGATTTGAGGGTTAATTATGATGATTTGAGGGTTAA
TTATGATCGCCTTTTACAAAACGCTTCGCCTTTATTAGAACTCTCTCAAAACACCACTTTTAAAATCTATCGCAAAG
CCTATCAAAAATCCTTACCTTTGTTGCGCACCATAAGGAGATGGGTTAAAAAATAA

SEQ ID NO 52

SEQ ID NO 59

Fig. 9A

GATGATTTGAGGGTTAATTAT SEQ ID NO 50
GATGATTTGAGGGTTAATTAT
GATGATTTGAGGGTTAATTAT
GATGATTTGAGGGTTAATTAT
GATGATTTGAGGGTTAATTAT
GATGATTTGAGGGTTAATTAT
GATGATTTGAGGGTTAATTAT

Fig. 9B

DLRVNYD SEQ ID NO 53
DLRVNYD
DLRVNYD
DLRVNYD
DLRVNYD
DLRVNYD
DLRVNYD

Fig. 9C

SEQ ID NO 78

PEPSPDPEPEPTPD
PEPSPDPEPEPSPD
PDP
DSDSDSDSGSDSDSGSDSDSESDSDSDSDSDSDSDSESDSDSESDSDSDSDSDSDSDSESDSDSDSDSDSDSD
SDSESDSDSESDSESDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSESDSDSDSDSDSDSDSDSDS
DSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDS
RVTPPNNEQKAPSN

Fig. 10D

SEQ ID NO 76

AATAATGAGAATGTTGTACGTTATGGTGGTGGAAGTGCTGATGGTGATTCAGCAGTAAATCCGAAAGACCCAACTCC
AGGGCCGCCGGTTGACCCAGAACCAAGTCCAGACCCAGAACCAGAACCAACGCCAGATCCAGAACCAAGTCCAGACC
CAGAACCGGAACCAAGCCCAGACCCGGATCCGGATTCGGATTCAGACAGTGACTCAGGCTCAGACAGCGACTCAGGT
TCAGATAGCGACTCAGAATCAGATAGCGATTCGGATTCAGACAGTGATTCAGATTCAGACAGCGACTCAGAATCAGA
TAGCGATTCAGAATCAGATAGCGACTCAGATTCAGATAGCGATTCAGATTCAGATAGCGATTCAGATTCAGATAGCG
ATTCGGATTCAGACAGTGATTCAGATTCAGACAGCGACTCAGAATCAGATAGCGACTCAGAATCAGATAGTGAGTCA
GATTCAGACAGTGACTCGGACTCAGACAGTGATTCAGACTCAGATAGCGATTCAGACTCAGATAGCGATTCAGATTC
AGACAGCGACTCAGATTCAGACAGCGACTCAGACTCAGATAGCGACTCAGACTCAGACAGCGACTCAGATTCAGATA
GCGATTCAGACTCAGACAGCGACTCAGACTCAGACAGCGACTCAGACTCAGATAGCGACTCAGATTCAGATAGCGAT
TCAGACTCAGACAGCGACTCAGATTCAGATAGCGATTCGGACTCAGACAGCGATTCAGATTCAGACAGCGACTCAGA
CTCGGATAGCGATTCAGATTCAGATAGCGATTCGGATTCAGACAGTGATTCAGATTCAGACAGCGACTCAGACTCGG
ATAGCGACTCAGACTCAGACAGCGATTCAGACTCAGATAGCGACTCAGACTCGGATAGCGACTCGGATTCAGATAGC
GACTCAGACTCAGATAGTGACTCCGATTCAAGAGTTACACCACCAAATAATGAACAGAAAGCACCATCAAATCCTAA
AGGTGAAGTAAACCATTCTAATAAGGTATCAAAACAACACAAAACTGATGCTTTACCA

Fig. 10A

SEQ ID NO 77

SEQ ID NO 54

AATAATCAGAATGTTGTACGTTATGGTGGTGGAAGTGCTGATGGTGATTCAGCAGTAAATCCGAAAGACCCAACTCC
AGGGCCGCCGGTTGAC
CCAGAACCAAGTCCAGACCCAGAACCAGAACCAACG
CCAGATCCAGAACCAAGTCCAGACCCAGAACCGGAA
CCAAGCCCAGACCCGGATCCG
GATTCGGATTCAGACAGT SEQ ID NO 55
GACTCAGGCTCAGACAGC SEQ ID NO 56
GACTCAGGTTCAGATAGC SEQ ID NO 57
GACTCAGAATCAGATAGC SEQ ID NO 58
GATTCGGATTCAGACAGT
GATTCAGATTCAGACAGC SEQ ID NO 59
GACTCAGAATCAGATAGC
GATTCAGAATCAGATAGC SEQ ID NO 60
GACTCAGATTCAGATAGC SEQ ID NO 61
GATTCAGATTCAGATAGC SEQ ID NO 62
GATTCAGATTCAGATAGC
GATTCGGATTCAGACAGT
GATTCAGATTCAGACAGC
GACTCAGAATCAGATAGC
GACTCAGAATCAGATAGT SEQ ID NO 63
GAGTCAGATTCAGACAGT SEQ ID NO 64
GACTCGGACTCAGACAGT SEQ ID NO 65
GATTCAGACTCAGATAGC SEQ ID NO 66
GATTCAGACTCAGATAGC
GATTCAGATTCAGACAGC
GACTCAGATTCAGACAGC SEQ ID NO 67
GACTCAGACTCAGATAGC SEQ ID NO 68
GACTCAGACTCAGACAGC SEQ ID NO 69
GACTCAGATTCAGATAGC
GATTCAGACTCAGACAGC SEQ ID NO 70
GACTCAGACTCAGACAGC
GACTCAGACTCAGATAGC
GACTCAGATTCAGATAGC
GATTCAGACTCAGACAGC
GACTCAGATTCAGATAGC
GATTCGGACTCAGACAGC SEQ ID NO 71
GATTCAGATTCAGACAGC
GACTCAGACTCGGATAGC SEQ ID NO 72
GATTCAGATTCAGATAGC
GATTCGGATTCAGACAGT
GATTCAGATTCAGACAGC
GACTCAGACTCGGATAGC
GACTCAGACTCAGACAGC
GATTCAGACTCAGATAGC
GACTCAGACTCGGATAGC
GACTCGGATTCAGATAGC SEQ ID NO 73
GACTCAGACTCAGATAGT SEQ ID NO 74
GACTCCGATTCAAGAGTT SEQ ID NO 75
ACACCACCAAATAATGAACAGAAAGCACCATCAAATCCTAAAGGTGAAGTAAACCATTCTAATAAGGTATCAAAACA
ACACAAAACTGATGCTTTACCA

Fig. 10B

Repeat pattern isolate 1:
1-2-3-4-1-5-4-6-7-8-8-1-5-4-9-10-11-12-12-5-13-14-15-7-16-15-14-7-16-7-17-5-18-8-1-5-18-15-12-18-19-20-21

Fig. 10E

TCAGCAGTAAATCCGAAAGACCCAACTCCAGGGCCGCCGGTTGACCCAGAACCAAGTCCAGACCCAGAACCAGAACC
AACGCCAGATCCAGAACCAAGTCCAGACCCAGAACCGGAACCAAGCCCAGACCCGGATCCG
GATTCGGATTCAGACAGT
GACTCAGGCTCAGACAGC
GACTCAGGTTCAGATAGC
GACTCAGAATCAGATAGC
GATTCGGATTCAGACAGT
GATTCAGATTCAGACAGC
GACTCAGAATCAGATAGC
GATTCAGAATCAGATAGC
GACTCAGATTCAGATAGC
GATTCAGATTCAGATAGC
GATTCAGAATCAGATAGC
GATTCGGATTCAGACAGT
GATTCAGATTCAGACAGC
GACTCAGAATCAGATAGC
GACTCAGAATCAGATAGT
GAGTCAGATTCAGACAGT
GACTCGGACTCAGACAGT
GATTCAGACTCAGATAGC
GATTCAGACTCAGATAGC
GATTCAGACTCAGACAGC
GATTCAGATTCAGACAGC
GACTCAGAATCAGACAGC SEQ ID NO 79
GACTCAGACTCAGATAGC
GACTCAGACTCAGACAGC
GACTCAGATTCAGATAGC
GATTCAGACTCAGACAGC
GACTCAGACTCAGACAGC
GACTCAGACTCAGATAGC
GATTCAGACTCAGACAGC
GACTCAGATTCAGATAGC
GATTCGGACTCAGACAGC
GATTCAGATTCAGACAGC
GACTCAGACTCGGATAGC
GATTCAGATTCAGACAGC
GACTCAGACTCGGATAGC
GACTCGGATTCAGATAGT SEQ ID NO 80
GACTCCGATTCAAGAGTT
ACACCACCAAATAATGAACAGAAAGCACCATCAAATCCTAAAGGTGAAGTAAACCATTCTAATAAGGTATCAAAACA
ACACAAAACTGATGCTTTACCAGAAACAGGAGATAAGAGCGAAAACACAAATGCAACTTTATTTGGTGCAATG

Fig. 10C

Repeat pattern isolate 2:
1-2-3-4-1-5-4-6-7-8-6-1-5-4-9-10-11-12-12-16-5-22-14-15-7-16-15-14-16-7-17-5-18-5-18-23-21

Fig. 10F